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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,588	12/12/2005	Tejal Ashwin Desai	140-05	7541

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EXAMINER

KOSAR, AARON J

ART UNIT	PAPER NUMBER
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1651

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10/26/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/535,588	Applicant(s) DESAI ET AL.	
	Examiner Aaron J. Kosar	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17, 20 and 26-28 is/are pending in the application.
- 4a) Of the above claim(s) 8-17, 20 and 26-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/26/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of group I, claims 1-7, in the reply filed on September, 18, 2007 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election/restriction requirement is still deemed proper and is therefore made FINAL.

Claims 8-17, 20, and 26-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 18, 2007.

Claims 1-7 are pending and have been examined on their merits.

Claim Objections

Claims 1-7 are objected to because of the following informalities: Claim 1 contains the trademark/trade name MATRIGEL. Where a trademark or trade name is used in the claims as a limitation to identify or describe an otherwise indescribable composition/product, in the instant case a particular laminin-collagen-heparin sulfate-entactin comprising composition, the trademarked name is required to appear in uppercase lettering. Please note, the use of trademarks in the claims would be rejectable under 35 U.S.C. 112, second paragraph, when the trademarked composition may be adequately and unambiguously described in generic terms. Though the Examiner has determined that MATRIGEL is sufficiently recognized in the art, to the extent that Applicant is capable of identifying the composition in generic terms (and which the specification provides support), Applicant is encouraged to use the generic terms where possible so as to avoid

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potential confusion or variability that may arise from the use of a trademarked composition in the claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims presently recite limitations that do not require any manipulation and/or isolation (e.g. tissue biopsy/histological preparation, isolated skeletal muscle, etc.) and, thus, may broadly and reasonably be interpreted as being drawn to products of nature.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: The associations among the layers of the “multilayer” microculture and the “plurality of layers”. Since the interrelations of the layers is a critical feature of the invention, and because the claims do not define how one layer relates to another, the combinations of layers, wherein each combination of layers potentially defines an independent invention, are limitless (e.g. plurality in a lateral distribution (microarray or multiwell plates)

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versus plurality in the vertical dimension (stacked layers), and combinations thereof). Because the cooperative relations of the elements are unclear, one would not be apprised as to the metes and bounds of the claims, rendering the claims indefinite.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-6, it is unclear what core elements define and distinguish a cell *type* and by what measure a cell *type* is defined in the instant invention. MPEP 2173.05(b) states that “a claim may be rendered indefinite by reference to an object that is variable” and “the addition of the word ‘type’ to an otherwise definite expression (e.g., Friedel-Crafts catalyst) extends the scope of the expression so as to render it indefinite” *Ex parte Copenhaver*, 109 USPQ 118 (Bd. App. 1955). Consequently, one would not be apprised as to the subject matter that Applicant intends to claim and would not be able to determine the metes and bounds of the claims, rendering the claims indefinite.

In claim 1, the term “width” refers to a relative unit of measure; however, the claims do not describe the three dimensional context in which the dimension of width is measured. Consequently, one would not be apprised as to the subject matter that Applicant intends to claim and would not be able to determine the metes and bounds of the claims, rendering the claims indefinite. This ground of rejection, however, may be overcome by amending the claims to recite the cooperative structural relationships as argued above for claims 1-7.

In claim 2, the phrase “distinct cell type” is unclear. The term “distinct” may refer to either (a) the association of cells between each of the layers (e.g. multiple layers each layer with

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cell types distinct versus the cell types in other layers) and/or (b) the limitation of the population of a particular layer (e.g. a limitation of “at least one” wherein each layer comprises *one* cell type, but not necessarily limiting the redundancy of a cell type among layers). Each is a reasonable interpretation of the claims, however each defines a different invention which embraces different subject matter. One would not be apprised as to what combination(s) Applicant intends to claim, rendering the metes and bounds of the claims indefinite.

In claim 5, the term “resistance” is a relative term which renders the claim indefinite. Whereas the term “resistance” is recited as referenced to a shear *flow rate* or 5µL/min flow rate, the associated shear *force* is dependent upon a myriad of properties including the cell-biopolymer fluid, the time of contact, and the total volume of contact. One of skill would not be apprised as to what defines resistant/non-resistance or gradations in between or how one would measure resistance *per se*. Because the claims do not provide a time or total volume of contact and do not define the nature or extent of shear which would (dis)qualify a composition as being resistant, the metes and bounds of the claims cannot be determined, rendering the claims indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over SINGVHI (US 5776748 (A: PTO-892 7/18/2007) or GRIFFITH (US 6,197,575 B1).

The claims are generally drawn to a multilayer microculture comprising (a) a plurality of layers, (b) at least one cell type per layer, (c) a biopolymer, and (d) a layer width less than 1 mm. The dependent claims are further drawn to the intrinsic properties of the composition and the identity of the cell(s) and a support material.

SINGVHI teaches a composition comprising a coated glass plate microculture, further comprising: multilayers (multiple monolayer islands/patterns); mammalian, non-contractile cells in each layer (*e.g.* primary rat hepatocyte); and a biopolymer (*e.g.* mouse laminin) (column 9, ¶1 ;column 10, ¶3; column 23, Ex.5). Singvhi also teaches that the size of the islands are preferably between 1 and 2,500 μm^2 , preferably between 1 and 500 μm^2 including lateral dimensions between 0.2 and 10 μm (column 3, ¶1).

GRIFFITH teaches a multilayer microculture comprising three dimensional networks; cells of one or more type, including endothelial and/or hepatocyte cells; and, a dimension of 75-1000 μm and volume comprising $1\text{cm}^2 \times 1\text{mm}$ (column 6, ¶2). Griffith also teaches “microtissues are layered together to form microscale tissue or micro-organ arrays.. and consist of tissues stacked on top of each other, side-by-side each other, or both..[and] may be interconnected or isolated”(column 6, ¶3). Additionally Griffith teaches a variety of cells (*e.g.* nerve cells, *etc.*: column 19, last ¶ and portion spanning column 20) and the attachment of cells to polystyrene Petri dishes coated with collagen (type I)(column 39).

SINGVHI is relied upon for the reasons discussed above. If not expressly taught by Singhvi, based upon the overall beneficial teaching provided by this reference with respect to individual dimensions in the manner disclosed therein, the adjustments of particular conventional working conditions (*e.g.*, determining one or more suitable dimensions for multiple layers in

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which to produce such a product), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

To the extent that Griffith is silent regarding the explicit combinations of the instant invention and claims, it would have been obvious to combine the elements to produce a multi-layered microculture as claimed, because Griffith teaches that a variety of methods may be used to create micromatrices including three-dimensional printing and that a variety of cells may be used (including cells which intrinsically secrete extracellular matrix (ECM) proteins).

Griffith is relied upon for the reasons discussed above. If not expressly taught by Griffith, based upon the overall beneficial teaching provided by this reference with respect optimal dimensions (column 3, ¶1) in the manner disclosed therein, the adjustments of particular conventional working conditions (e.g., determining one or more suitable dimensions in which to produce such a product), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.


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Conclusion


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aaron J. Kosar whose telephone number is (571) 270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Aaron Kosar
Examiner, Art Unit 1651



SANDRA E. SAUCIER
PRIMARY EXAMINER